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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,303	11/04/2005	Peter Bernstein	133087.12001(100819-1PUS)	5966

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EXAMINER	
O DELL, DAVID K	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
04/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,303	BERNSTEIN ET AL.	
	Examiner	Art Unit	
	David K. O'Dell	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,24 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-4, 6, 7, 24 and 25 are pending in the current application.

2. The instant application is a 371 of PCT/SE2003/001329, filed August 26, 2003, which claims the priority of Application No. 0202567-4 filed in Sweden on August 29, 2002 and Application No. 0202986-6 filed in Sweden on October 9, 2002.

Claim Rejections/Objections Withdrawn

3. The rejections of canceled claims are withdrawn.

Claim Rejections/Objections Maintained/ New Grounds of Rejection

4. The rejection of claims 1-4, 6, 7, 24 and 25 under 35 U.S.C. 103(a) as being obvious over Harrison et. al. U. S. patent 5,620,989 AND Stevenson, Graeme I. et. al. "4,4-Disubstituted Piperidine High-Affinity NK1 Antagonists: Structure-Activity Relationships and in Vivo Activity" *Journal of Medicinal Chemistry*, **1998**, *41*, 4623-4635 in view of Bernstein et. al. "Discovery of Novel, Orally Active Dual NK1/NK2 Antagonists" *Bioorganic and Medicinal Chemistry Letters* **2001** *11*, 2769-2773 and Elliot et. al. *Bioorganic & Medicinal Chemistry Letters* **2002**, 12, 1755–1758. Applicant's arguments filed on November 19, 2008 have been fully considered but they are not persuasive. With respect to the 103 (a) rejection, the applicant has argued the references individually in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The applicant has alleged that two changes are taking place to these compounds over the prior art Stevenson and Harrison compounds, however this is not the case. These changes may be viewed

as a replacement of the O-Bn of Harrision with a naphthyl amide, or as analogs of the Stevenson by the substitution of benzylamine with a naphthyl amide. The napthylamide is taught by Bernstein et. al. thus the analysis does not require two changes as the applicant has suggested. The applicant has further suggested that the Elliot et. al. is not applicable since the compounds are of different structure, however this is not persuasive since the compounds of Elliot et. al. are clearly strucuturally similar as highlighted in the Figure 1 of the examiner. If in fact Elliot et. al. were working on a different receptor, a different biological target, this argument would be very persuasive, however the facts are that all the documents cited including Elliot et. al. pertain to the NK1 receptor. One working in this field would have been immediately be aware of these teachings and the relevance to the compounds. Remarkably the applicant has suggested that Elliot et. al. is actually directing one to the propyl linkers not amides, however this is not the case as he Elliot states "relatively poor affinity of the propyl linker 24 (hNK1IC50 40nM) shows that a heteroatom in the chain is beneficial." The examiner requests clarification in the next communication as to how the Elliot et. al. reference shows a preference for propyl.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the very close structurally similarity and guidance present in the art show that the invention is obvious over the prior art.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

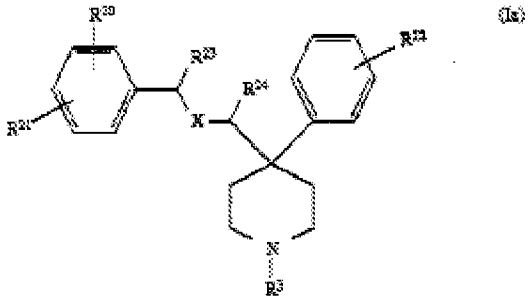
4. Claims 1-4, 6, 7, 24, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et. al. U. S. patent 5,620,989 AND Stevenson, Graeme I. et. al. "4,4-Disubstituted Piperidine High-Affinity NK1 Antagonists: Structure-Activity Relationships and in Vivo Activity" *Journal of Medicinal Chemistry*, **1998**, *41*, 4623-4635 in view of Bernstein et. al. "Discovery of Novel, Orally Active Dual NK1/NK2 Antagonists" *Bioorganic and Medicinal Chemistry Letters* **2001** *11*, 2769-2773 and Elliot et. al. *Bioorganic & Medicinal Chemistry Letters* **2002**, 12, 1755–1758. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Determination of the scope and content of the prior art

(MPEP 2141.01)

Harrison et. al. teaches NK-1 antagonists that are analogs of the compounds of the instant case that have the same utility. In particular the genus shown below:

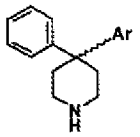
A particular sub-class of compounds according to the invention is represented by compounds of formula (Ia), and salts and prodrugs thereof:

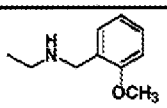
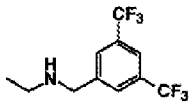
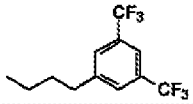


(Ia)

Stevenson et. al. teach piperidinyl phenyl amide compounds that are remarkably similar in structure and have the same utility. In particular the compounds on page 4630 Table 4:

Table 4. Alternative Linkers



Compound	Ar	hNK1 IC_{50}[a]	Formula	Analysis
48		> 100[b]	$C_{20}H_{22}N_2O$	C, H, N
49		12.6 ± 8.8	$C_{21}H_{22}N_2F_6$	C, H, N
57		63 ± 7	$C_{22}H_{23}NF_6$	C, H, N[c]

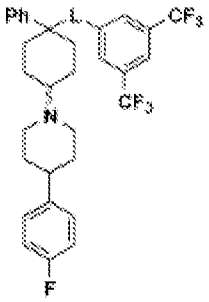
[a] Displacement of [^{125}I]-labeled substance P from the cloned receptor expressed in CHO cells ($n = 3$). [b] 31% and 25% @ 0.1 μM. [c] $C_{22}H_{23}NF_6$ requires 415.1734, found 415.1750.

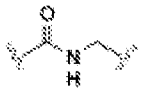
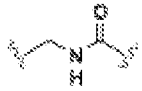
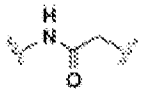
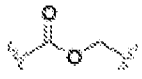
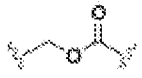
. Elliot et. al. in his NK-1 antagonists, teaches that a variety of moieties can be used to link the 4,4-disubstituted piperidine carbon to an aryl group.

"Table 1 summarises the effect of modifications to the amide linker of 2. Throughout, trans-isomers have

higher affinity than the corresponding cis-isomers**. A number of different linkers are tolerated, most notably the amides 2 and 15, the amine 17 and ether 23.** The relatively poor affinity of the propyl linker 24 (hNK_1 IC_{50} 40nM) shows that a heteroatom in the chain is beneficial. This could be because the heteroatom introduces a conformational bias which favours binding, or due to participation of the heteroatom in a hydrogen bond to the receptor." Pg. 1756-1757 Bioorganic & Medicinal Chemistry Letters 12 (2002) 1755–1758

Table 1. Linker replacements



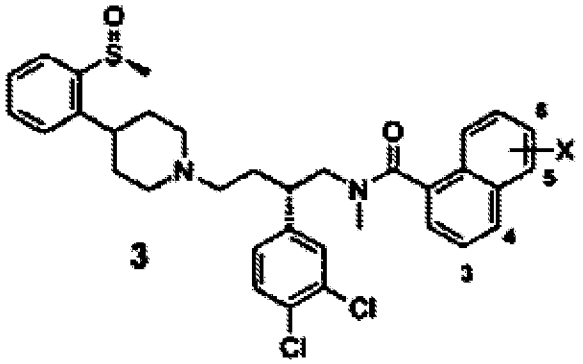
Compd	-L-	Stereochemistry	hNK$_1$ IC$_{50}$ (nM)[a]
11		*cis*-	150 ± 80
2		*trans*-	0.34 ± 0.10
12		*cis*-	250 ± 26
13		*trans*-	6.3 ± 2.5
14		*cis*-	85 ± 46
15		*trans*-	0.70 ± 0.44
16		*cis*-	82 ± 0
17		*trans*-	1.7 ± 0.6
18		*cis*-	140 ± 49
19		*trans*-	2.5 ± 0.6
20		*cis*-	50% @ 1000
21		*trans*-	120 ± 99
22		*cis*-	59 ± 18
23		*trans*-	4.2 ± 1.9
24		1:1 *cis*- and *trans*-	40 ± 3

[a]Displacement of [^{125}I]-labelled substance P from the cloned receptor expressed in CHO cells. Data are mean ± SD ($n = 3$).[5]

Bernstein et. al. "Discovery of Novel, Orally Active Dual NK1/NK2 Antagonists" *Bioorganic and Medicinal Chemistry Letters* **2001** *11*, 2769-2773, teaches the exact modification (down to the very precise substituents on the naphthyl ring), thus the use of naphthyl in these NK1-

antagonists and the substitution of naphthyl for phenyl was very well known even in this very small field. Starting with the known selective antagonist SR48968, Bernstein modified the phenyl portion by screening a diverse set of compounds where the phenyl was replaced with "over 100 aryl, heteroaryl and arylalkyl groups". In the words of Bernstein the result of this study was "the most potent, dual acting compound to come out of this array was the naphthamide **2a**". Bernstein goes on to describe that "to follow-up the discovery of this naphthamide we explored the effect of substituents on the naphthalene ring."

Table 2. Exploration of varying substituents in 3-X-naphthamides



Compd	3 X=	pK_B[a] NK_1	pK_B[a] NK_2	Dose ratio[b]	
				NK_1	NK_2
2a	H	7.89±0.08	8.18±0.28	52	262
3b	NO_2	8.16±0.10	9.03±0.18	50	321
3c	Br	8.15±0.34	7.67±0.24	43	34
3d (ZD6021)	C≡N	8.98±0.17	8.26±0.10	144	74
3e	SO_2CH_3	7.43±0.25	7.35±0.04	22	28
3f	Cl	7.15±0.12	7.10±0.09	13	31
3g	OMe	7.95±0.04	7.70±0.06	47	77
3h	CO_2H	5.68±0.14	6.86±0.11	ND[c]	ND
3i	CH_3	8.03±0.04	7.29±0.21	26	123
3j	CH_2CN	8.42±0.24	6.99±0.06	133	39
3k	Ac	7.41±0.35	7.17±0.13	41	156
3l	$C(=CH_2)CH_3$	7.24±0.19	7.24±0.29	31	75
3m	SO_2NH_2	7.54±0.04	7.02±0.21	170	7
3n	$CON(Me)_2$	5.17±0.22	7.31±0.33	ND	ND
3o	C≡CH	7.71±0.14	7.44±0.22	23	34
3p	F	7.90±0.07	8.15±0.23	12	52
3q	CF_3	7.84±0.07	6.45±0.25	ND	ND

It is interesting that 3-cyano-naphthyl amide was the preferred substituent, as in compound **4**. This 3-cyano naphthyl amide group is also the preferred substituent of the instant case and is

what distinguishes these compounds from those of Stevenson et. al. and Harrison. There can be no doubt that this was the preferred substituent.

The difference between the prior art and the claims

The instant claims differ from the compounds of Stevenson et. al only in the substitution of a naphthoyl group for the benzyl group of Stevenson. These changes may also be viewed as a replacement of the O-Bn of Harrision with a naphthyl amide, or as analogs of the Stevenson the substitution of benzylamine with a napthamide. This is shown below in Figure 1.

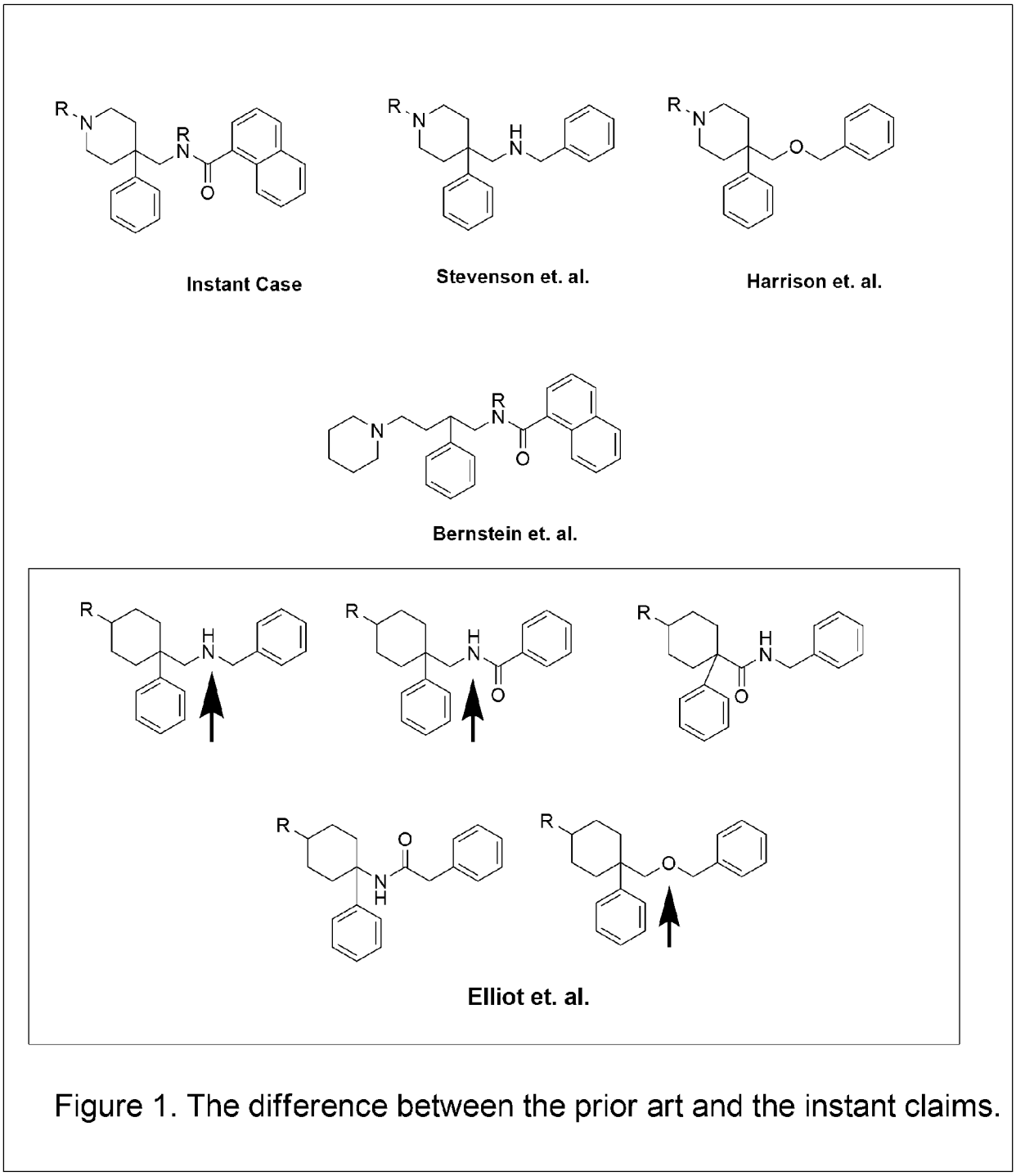


Figure 1. The difference between the prior art and the instant claims.

(MPEP 2141.02)

Stevenson et al. and Harrison et. al. do not expressly teach the exact compounds of the instant case.

Finding of prima facie obviousness

Rational and Motivation
(MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use analogs of those of Harrison and Stevenson et. al. to produce the instant invention. Analogs differing only in the substitution of phenyl for naphthyl, are *prima facie* obvious, and require no secondary teaching when the utility is the same. The other difference the use of a different linker between the piperidine ring and the phenyl group, which are taught by Elliot as being equivalent. The experienced Ph.D. synthetic organic chemist, who would make Applicants' compounds, would be motivated to prepare these compounds on the expectation that such close analogues would have similar properties and upon the routine nature of such experimentation in the art of medicinal chemistry. It would be routine for the chemist to replace phenyl with naphthyl especially since the chemistry developed by Stevenson was in place and the synthesis only involved using an appropriate naphthyl halide (see scheme 5 of Stevenson et. al.), moreover Stevenson suggests that lipophilicity of the aryl moiety to be important since compound **49** bearing the lipophilic CF_3 group has increased potency over compound **48** (see table 4 above), thus naphthyl being slightly more lipophilic would have increased potency. Naphthyl and more specifically, the 3-cyano naphthyl group is also the preferred substituent of Bernstein et. al. who showed the preference for naphthyl over phenyl. There can be no doubt that this was the preferred substituent.

Ex parte WESTFAHL, 136 USPQ 265 (Bd. Pat. App. & Int. 1962):

> "Appellant relies upon the case of In re Jones, 32 CCPA 1020, 1945 C.D. 304, 579 O.G. 148, 149 F.2d 501, 65 USPQ 480 , as supporting the patentability of claim 8 because in that case a naphthyl compound was held to be patentable over the corresponding phenyl compound. However, the rejection in that case was based upon the premise, held to be untenable by the court, that benzene and naphthalene are members of a homologous series. In the present case, **the examiner does not rely upon any theory of homology but has cited a reference (Richter II) teaching that naphthalene is very similar to benzene and forms a series of analogous derivatives**."

The fact that Stevenson didn't use amides, is a non-issue since Elliot et. al. in his NK-1 antagonists replaced amino groups with amides and they were all "tolerable". It would be routine for the chemist to make the amides especially since the chemistry developed by Stevenson was in place and the synthesis only involved using an appropriate naphthyl halide or acid (see scheme 5 of Stevenson et. al.), moreover Stevenson suggests that compounds with an amino nitrogen that is too basic are less active. It goes without saying that the amino nitrogen is substantially more basic than an amide. In fact an amide is somewhat acidic. Furthermore Elliot et. al. teaches that they are in fact interchangeable.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One of ordinary skill is also one of "ordinary creativity, not an automaton". See Leapfrog Enterprises Inc. v. Fisher-Price. and Mattel Inc. UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT "An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 550 U.S. , 2007 U.S. LEXIS 4745, 2007 WL 1237837, at 12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

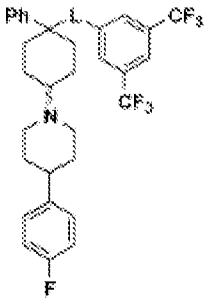
6. Claims 1-4, 6, 7, 24 and 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending

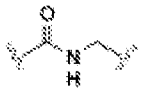
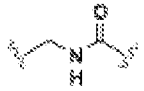
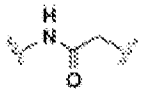
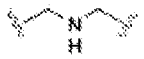
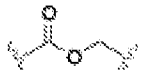
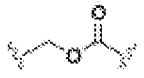
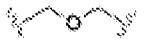
Application No. 10/539,140 in view of Elliot et. al. Bioorganic & Medicinal Chemistry Letters 12 (2002) 1755–1758.

This is a provisional obviousness-type double patenting rejection. The instant claims differ from those of the '140 application by the identity of the moiety linking the naphthyl ring to the piperidine. This change is taught by Elliot et. al. in his NK-1 antagonists.

"Table 1 summarises the effect of modifications to the amide linker of 2. Throughout, trans-isomers have higher affinity than the corresponding cis-isomers. **A number of different linkers are tolerated, most notably the amides 2 and 15, the amine 17 and ether 23.** The relatively poor affinity of the propyl linker 24 (hNK_1 IC_{50} 40nM) shows that a heteroatom in the chain is beneficial. This could be because the heteroatom introduces a conformational bias which favours binding, or due to participation of the heteroatom in a hydrogen bond to the receptor." Pg. 1756-1757 Bioorganic & Medicinal Chemistry Letters 12 (2002) 1755–1758

Table 1. Linker replacements



Compd	-L-	Stereochemistry	hNK$_1$ IC$_{50}$ (nM)[a]
11		*cis*-	150 ± 80
2		*trans*-	0.34 ± 0.10
12		*cis*-	250 ± 26
13		*trans*-	6.3 ± 2.5
14		*cis*-	85 ± 46
15		*trans*-	0.70 ± 0.44
16		*cis*-	82 ± 0
17		*trans*-	1.7 ± 0.6
18		*cis*-	140 ± 49
19		*trans*-	2.5 ± 0.6
20		*cis*-	50% @ 1000
21		*trans*-	120 ± 99
22		*cis*-	59 ± 18
23		*trans*-	4.2 ± 1.9
24		1:1 *cis*- and *trans*-	40 ± 3

[a]Displacement of [^{125}I]-labelled substance P from the cloned receptor expressed in CHO cells. Data are mean ± SD (n = 3).[5]

They are all "tolerated" according to Elliot.

It would have been obvious to one of ordinary that the amide analogs of the instant case would be active as taught by Elliot et. al. The experienced Ph.D. synthetic organic chemist, who would make Applicants' compounds, would be motivated to prepare these compounds on the

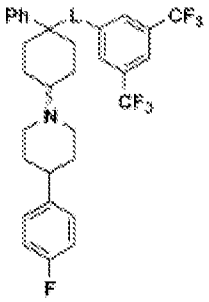
expectation that such close analogues would have similar properties and upon the routine nature of such experimentation in the art of medicinal chemistry. It would be routine for the chemist to change the linker. Elliot et. al. teaches that they are in fact interchangeable.

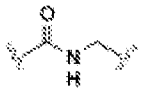
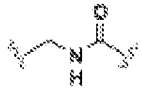
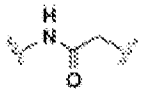
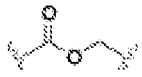
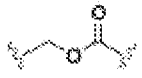
7. Claims 1-4, 6, 7, 24 and 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/527,280, in view of Elliot et. al. Bioorganic & Medicinal Chemistry Letters 12 (2002) 1755–1758.

This is a provisional obviousness-type double patenting rejection. The instant claims differ from those of the '280 application by the identity of the moiety linking the naphthyl ring to the piperidine. This change is taught by Elliot et. al. in his NK-1 antagonists.

"Table 1 summarises the effect of modifications to the amide linker of 2. Throughout, trans-isomers have higher affinity than the corresponding cis-isomers. **A number of different linkers are tolerated, most notably the amides 2 and 15, the amine 17 and ether 23.** The relatively poor affinity of the propyl linker 24 (hNK_1 IC_{50} 40nM) shows that a heteroatom in the chain is beneficial. This could be because the heteroatom introduces a conformational bias which favours binding, or due to participation of the heteroatom in a hydrogen bond to the receptor." Pg. 1756-1757 Bioorganic & Medicinal Chemistry Letters 12 (2002) 1755–1758

Table 1. Linker replacements



Compd	-L-	Stereochemistry	hNK$_1$ IC$_{50}$ (nM)[a]
11		*cis*-	150 ± 80
2		*trans*-	0.34 ± 0.10
12		*cis*-	250 ± 26
13		*trans*-	6.3 ± 2.5
14		*cis*-	85 ± 46
15		*trans*-	0.70 ± 0.44
16		*cis*-	82 ± 0
17		*trans*-	1.7 ± 0.6
18		*cis*-	140 ± 49
19		*trans*-	2.5 ± 0.6
20		*cis*-	50% @ 1000
21		*trans*-	120 ± 99
22		*cis*-	59 ± 18
23		*trans*-	4.2 ± 1.9
24		1:1 *cis*- and *trans*-	40 ± 3

[a]Displacement of [^{125}I]-labelled substance P from the cloned receptor expressed in CHO cells. Data are mean ± SD (n = 3).[5]

This is a provisional obviousness-type double patenting rejection.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.

/Rita J. Desai/
Primary Examiner, Art Unit 1625